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(54) Title: SUPERCRITICAL HYDROGENATION

(57) Abstract

A process for the selective hydrogenation of aliphatic or aromatic substrates under supercritical or near critical conditions. Hydrogenation is effected using a heterogeneous catalyst in a continuous flow reactor containing a supercritical or near critical reaction medium and selectively product formation is achieved by varying one or more of the temperature, pressure, catalyst and flow rate.

SUPERCRITICAL HYDROGENATION

The present invention relates to a method of hydrogenating organic compounds. More specifically, the present invention relates to heterogeneous catalytic hydrogenation of organic compounds under conditions of continuous flow of the reactants.

Hydrogenation is a commercially very significant process and enjoys widespread use in the food industry to produce amongst other things edible oils and spreads, and in the fine chemicals, plastics, pharmaceuticals and agricultural industries as a synthetic tool.

Although the use of supercritical fluids as reaction media has been disclosed for a limited number of synthetic organic reactions, the synthetic uses disclosed so far have involved heterogeneous or homogeneous batch systems or homogeneous continuous flow systems and suffer a number of disadvantages.

Catalytic hydrogenation under supercritical conditions is known from WO 94/06738 which discloses a process for manufacturing alcohols by liquid phase heterogeneous catalytic hydrogenation of mono- or dicarboxylic acids or their esters in a liquid inert hydrogen carrier such as a hydrocarbon. In this patent, hydrogenation is preferably carried out under supercritical conditions and is performed in a fixed-bed reactor or a batch autoclave. The process requires a high ratio of hydrogen with respect to the material to be hydrogenated and this is achieved by decreasing the concentration of the starting material in the reaction medium. The alcohol product is separated from dissolved hydrogen on depressurising the mixture. The presence of such an excess of hydrogen presents an explosion risk and is therefore unacceptable for large scale synthesis, unless of course the quantity of carboxylic acid is decreased to such an extent that the

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amount of hydrogen present does not pose a significant
risk. However in this case the quantity of carboxylic
acid which can be hydrogenated renders the process
useless for large scale synthesis.

5   The Journal of the American Chemical Society 1995,
117 (31), 8277 discloses asymmetric catalytic
hydrogenation reactions in supercritical carbon dioxide
using a homogenous chiral rhodium catalyst in a batch-
type process. A small-scale reactor is charged with
10   the compound to be hydrogenated and carbon dioxide at a
pressure of approximately 3000psig and hydrogen gas at
200psig. Significant enantiomeric excesses are claimed
for hydrogenations performed under these conditions but
the product nevertheless requires purification to
15   separate the catalyst from the product after reaction.
        EP-A-0652202 discloses a method for producing
formic acid or formic acid derivatives in a reaction
employing carbon dioxide in the supercritical state as
the reaction medium. The reaction may be performed in
20   the presence of a homogeneous or heterogeneous
catalyst. In this patent, the supercritical carbon
dioxide medium represents one of the reactants and is
consumed during the process. The carbon dioxide is
mixed with hydrogen at a relatively high pressure to
25   produce formic acid, or with an active hydrogen group-
containing compound to produce a formic acid derivative
in a continuous process.
        A method for the direct oxidation of benzene or
other aromatic hydrocarbons into phenols is disclosed
30   in WO 9420444. In this method, the aromatic
hydrocarbon is dissolved in a mixture of supercritical
carbon dioxide, molecular oxygen, and hydrogen as a
reducing gas. The oxidation is performed under
pressure in the presence of a palladium-containing
35   catalyst and the reaction mixture is homogenous, hence
avoiding the use of an inefficient 2-phase system. The

carbon dioxide separated from the reaction mixture is vapourised and may be re-used in the oxidation of a new batch of aromatic hydrocarbons.

WO 9522591 discloses a process for the continuous hydrogenation of unsaturated fats, fatty acid or fatty acid esters under supercritical conditions on a shaped platinum-group metal catalyst in a solid bed constructed from an inert support and finely divided catalyst. The supercritical medium and the inert support are mixed in the free space above the catalyst in the reaction chamber in order to avoid any pressure drop in the supercritical fluid. The process is said to give considerably improved activity and selectivity in the hydrogenation reaction when compared to conventional trickle bed hydrogenation processes.

A number of patents, for example DE 3133723, DE 3133562 and US 4354922 disclose the hydrocracking of coal using supercritical water as the solvent. In these patents, the hydrocarbon components of coal are degraded under the reaction conditions to produce lighter hydrocarbons hence the reaction conditions do not represent synthetically viable conditions for conventional hydrogenation reactions.

The various reaction systems described above suffer a number of disadvantages, for example waste solvent and unconsumed reactants are associated with each completed batch in a batch type process. Furthermore, in a batch type process, there is the possibility that the products obtained will be a mixture of both the kinetic reaction products and the thermodynamic reaction products unless the reaction conditions are carefully controlled to exclude one or other of these.

Although a continuous flow homogenous system overcomes this problem because the product can be withdrawn as it is formed, this type of process suffers

the disadvantage that the catalyst and the reaction
products must be separated from the reaction mixture.
In addition, the reactants and reaction products in
this type of continuous flow process are exposed to the
5   catalyst for a period which cannot easily be defined,
in contrast to a batch type process in which the
contact time is carefully controlled. Thus the
starting material or products in a continuous flow
reaction of this type may suffer undesirable side
10   reactions. For the same reason, this type of
continuous flow process is difficult to model and
therefore does not allow an accurate prediction of the
likely products, or an indication as to the likely
reaction time or extent of reaction.

15   Previously, attempts to vary the parameters of
reactions of this type have resulted in a loss of
product selectivity and have not therefore been viable.
For example, increasing the temperature would result in
loss of hydrogen from the solution and a consequential
20   loss in selectivity in a mass-transport-controlled
reaction.

             Accordingly, there is a need for a hydrogenation
process which can be effected under conditions such
that only small quantities of the organic compound and
25   hydrogen are required in the reactor at any one time,
and yet which can be used on an industrial scale for
the manufacture of hydrogenated products. In addition,
because undesirable side reactions or incomplete
conversion of the reactants represent a waste of
30   resources, there also remains a need for a
hydrogenation process which allows careful control of
the product formation and a decreased incidence of side
products. There is also a need for a process in which
wasted reaction time, and hence lost yield can be
35   minimised by decreasing the 'downtime' of the process.
             According to the present invention, there is

provided a process for the selective hydrogenation of
one or more functional groups in an organic compound
wherein the functional group is selected from: alkene,
cyclic alkene, cyclic alkane, lactone, anhydride,
amide, lactam, Schiffs base, aldehyde, ketone, alcohol,
nitro, hydroxylamine, nitrile, oxime, imine, azine,
hydrazone, aniline, azide, cyanate, isocyanate,
thiocyanate, isothiocyanate, diazonium, azo, nitroso,
phenol, ether, furan, epoxide, hydroperoxide, peroxide,
ozonide, arene, saturated or unsaturated heterocycle,
halide, acid halide, acetal, ketal, and a selenium or
sulfur containing compound, wherein the process
consists of continuously hydrogenating the compound
over a heterogeneous catalyst where at least one of the
components, in addition to hydrogen is under
supercritical or near critical conditions, and wherein
one or more of temperature, pressure, catalyst, flow
rates and hydrogen concentration are controlled so as
to effect selective hydrogenation.

The present invention solves the above problems by
effecting hydrogenation of organic compounds under
conditions close to or above the supercritical point of
the reaction medium in the presence of a heterogeneous
catalyst in a continuous flow reactor. It will, of
course, be appreciated that hydrogen may be replaced by
an isotope of hydrogen (for example to effect
deuteration reactions), or by a hydrogen transfer agent
(for example, formic acid).

The organic compound is hydrogenated in a
continuous process which comprises the steps of:

(a) admixing a supply of an inert fluid with a
supply of a first organic compound and a supply of
hydrogen;

(b) adjusting the temperature and pressure of the
resulting admixture to pre-determined values of
temperature and pressure close to or above the critical

point of the fluid to produce a reaction mixture from
which substantially a single desired product is formed
from amongst a plurality of possible products which may
be formed by hydrogenation of the first organic

5　　compound in a selective reaction, wherein the choice of
the pre-determined values is dependent on which of the
possible products is to be formed by reaction;

　　　　(c)　exposing the reaction mixture to a
heterogeneous catalyst to facilitate the selective

10　　reaction; and

　　　　(d)　removing the reaction mixture after reaction
from the region of the catalyst and isolating the
desired product by depressurisation of the reaction
mixture.

15　　　　The heterogeneous continuous flow system of the
present invention offers a number of advantages
compared with batch type systems or a homogenous
continuous flow system.　In particular, the present
invention allows the formation of a desired end product

20　　in a selective manner by controlling one or more of:
the temperature, the pressure of the reaction, by
varying the catalyst used for a given set of reagents,
and the flow rate through the apparatus.　The factors
controlling the selectivity of hydrogenation will

25　　depend on the particular reaction and in some instances
the temperature or the pressure will be the controlling
factor, whereas in other cases the catalyst or flow
rate may be more important in determining the outcome
of the reaction.　Suitable conditions for a given

30　　substrate and desired product are thus determined in
accordance with the present invention.

　　　　In an embodiment, the apparatus has two or more
reaction zones placed in series with regard to each
other, each reaction zone optionally being at a

35　　different temperature, for performing different
hydrogenation reactions.　Thus, a primary or secondary

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amine may be formed in situ by reduction of an azo, hydrazone, nitroso, nitro, oximino, hydroxylamine or nitrile group. For example, the first reaction zone may contain a catalyst for effecting reduction of a

5 nitro compound to an amine using, for example, a palladium catalyst, and the second zone may contain, for example, a nickel catalyst for effecting reductive alkylation of the amine formed in the first zone. In this particular case, the two zones are under the same

10 conditions of temperature and pressure with the two zones containing different catalysts to control the reaction. Similarly, a carbonyl compound may be formed in situ in the first reactor from an acetal or ketal and subsequently reacted in the second reactor.

15 The present invention also offers the advantage that hazardous reagents may be used without the need for a high inventory of reagent at any one time, since the organic compound and hydrogen are continuously fed to the reactor. Similarly, the product is collected

20 continuously from the reactor and does not therefore accumulate in large quantities in the reactor where it may suffer degradation. There is also a concomitant increase in the safety of the process as compared to a batch-process when using hazardous reagents or when

25 forming hazardous products since these materials are not usually present in sufficient quantities to represent a significant risk. Since the continuous flow process of the present invention also allows cleaner reactions to be performed than those of a

30 corresponding batch-type process, the cost of purifying the products is reduced. Furthermore, the continuous flow process of the present invention does not require separation of the reaction product from the catalyst, as is the case in a process employing a homogenous

35 catalyst.

The present invention has the further advantage of

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providing higher yields and higher throughputs than
conventional methods. Whilst the actual throughputs
will inevitably depend on the particular reaction
employed and the size of the apparatus, throughputs of
5   25 mls per minute or higher are attainable using
laboratory scale apparatus. Furthermore, selectivities
in excess of 85% can easily be achieved using the
process of the present invention.

Hydrogenation according to the present invention
10   is performed close to or above supercritical point of
the desired medium. Any fluid having a supercritical
point may be employed for the process of the present
invention. However, in practice the choice of fluid
will depend upon the solubility of the organic compound
15   in the fluid since a function of the supercritical or
near-critical fluid is to act as a solvent for the
organic compound and the hydrogen. It is also
important that the reaction medium is inert with
respect to the reactants and the product of the
20   reaction in order to avoid undesirable side reactions.

The term hydrogenation in the context of the
present invention is also intended to include reactions
such as reductive ammination, reductive coupling and
reductive alkylation, since these reactions all require
25   a source of H_2 in addition to a second organic compound
in order to effect reduction.

Particularly favoured media include carbon
dioxide, sulphur dioxide, alkanes such as ethane,
propane and butane, and halocarbons such as
30   trichlorofluoromethane, dichlorofluoromethane,
dichlorodifluoromethane, chlorotrifluoromethane,
bromotrifluoromethane, trifluoromethane, and
hexafluoroethane. The reaction medium may be a mixture
of two or more fluids having critical points which do
35   not require commercially unacceptable conditions of
temperature and pressure in order to achieve the

necessary conditions for reaction according to the
present invention. For example, mixtures of carbon
dioxide with an alkane such as ethane or propane, or a
mixture of carbon dioxide and sulphur dioxide may be
5   employed close to or above their theoretical critical
points.

In the context of the present invention, the lower
limit of the conditions suitable for supporting the
hydrogenation reaction are conditions of temperature
10   and pressure below and near the critical point. When a
fluid reaches its critical point its density is
substantially decreased relative to its density at its
boiling point at normal pressure. Small changes in
pressure near the critical point cause additional
15   changes in density. The process will operate in the
fluid at temperatures and pressures below the critical
point but at which the density of the fluid is
sufficient to ensure that the substrate and hydrogen
are substantially in a single phase.

20   The upper limit of temperature and pressure is
governed by limitations of the apparatus. It is also a
feature of the present invention that variation of the
physical conditions of the reaction may be used to
control the product of the hydrogenation.

25   Particular organic compounds which lend themselves
to the process of the present invention include the
heterogeneous catalysed reduction of cyclic alkanes,
arenes, alkenes, alkynes, organic halides, amines,
nitro compounds, ethers, alcohols and phenols,
30   aldehydes and ketones, sulphur-containing compounds,
selenium-containing compounds, acid halides, nitriles,
amides, cyclic anhydrides, anhydrides, epoxides,
nitroso compounds, oximes, azides, isocyanates,
isothiocyanates, diazonium compounds, hydroperoxides,
35   peroxides, saturated or unsaturated heterocycles, and
Schiff bases. Heterogeneous catalysed reductive

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process such as reductive coupling, reductive amination and reductive alkylation are also easily performed according to the process of the present invention. Likewise, heterogeneous catalytic hydrogenolysis of alkyl halides, aryl halides, acyl halides, alcohols and amine oxides may also be performed according to the process of the present invention. Although aliphatic compounds are more difficult to hydrogenate than aromatic compounds under the reaction conditions employed in the present invention, the hydrogenation of both aliphatic and aromatic compounds is possible according to the present invention.

Table 1 shows typical conditions for a variety of hydrogenation reactions performed according to the present invention.

Table 1

Substrate	Sub. Flow [ml/min]	Solvent	Flow [l/min]	Catalyst	Substr. :H₂	P_R [bar] Sol.+H₂	T [°C]	Products % (analysis by GC (external standards) except when marked with # where analysis is by NMR)
Cyclo-hexene								Cyclo-hexane
(0.2)	0.5-20.0	CO_2	0.75-1.65	5% Pd	1:2-4	120-140	40-320	(98)
(0.3)	0.5-2.0	propane	0.75	5% Pd, Pt	1:2	60-80	100-170	(96)
1-Octyne*	0.5-1.0	CO_2	0.75	5% Pd	1:4	120	>40	Octane (99.5) 1-Octene (0.02) *(0.02)
1-Octene	0.5-10.0	CO_2	1.0	5% Pd	1:2	120	>40	Octane (quant.)#

Substrate	Sub. Flow	Solvent	Flow	Catalyst	Substr.:H₂	P_R	T	1-phenyl-ethanol	Ethyl-benzene	1-cyclo-hexyl-ethanol	Ethyl-cyclo-hexane	Cyclo-hexane
Aceto-phenone												
(3)	0.5	CO_2	1.0	5% Pd	1:2	120	90	(85)	(7)	(0)	(0)	(0)
(0)#	0.5	CO_2	1.0	5% Pd	1:5	120	180	(14)#	(41)#	(28)#	(17)#	(0)#
(8)	1.0	CO_2	1.0	5% Pd	1:3	120	200	(0)	(70)	(0)	(17)	(0)
(6)	0.5	CO_2	1.0	5% Pd	1:6	120	300	(0)	(4)	(1)	(88)	(1)

Substrate	Sub. Flow	Solvent	Flow	Catalyst	Substr.:H₂	P_R	T	Benzyl-alcohol	Toluene	cyclo-hexyl-methanol	Methyl-cyclo-hexane	Cyclo-hexane
Benzal-dehyde												
(0)#	0.5	CO_2	1.0	5% Pd	1:2	120	95	(92)#	(8)#	(0)#	(0)#	(0)#
(0)#	0.5	CO_2	1.0	5% Pd	1:4	120	140	(18)#	(77)#	(4)#	(1)#	(0)#
(0)#	1.0	CO_2	1.0	5% Pd	1:6	120	180	(22)#	(59)#	(10)#	(7)#	(1)#
(0)#	0.5	CO_2	1.0	5% Pd	1:8	120	270	(1)#	(22)#	(3)#	(40)#	(25)#

Table 1

Substrate	Sub. Flow [ml/min]	Solvent	Flow [l/min]	Catalyst	Substr.:H₂	P_R [bar] (Sol.+H₂)	T [°C]	Products % (analysis by GC (external standards) except when marked with # where analysis is by NMR)			
								Aniline	Amino-cyclo-heane	Dicyclohexylamine	Cyclo-hexane
Nitro-benzene											
	0.5	propane	0.75	1% Pd	1:6	80	150-200	(97)	(0)	(0)	(0)
	0.3	propane	0.75	5% Pd	1:9	80	200-250	(9)	(29)	(58)	(1)
1,2-(Methylenedioxy)-4-nitrobenzene *Starting material dissolved in a mixture of MeOH and THF, flow of solution: 10 ml min⁻¹*								1,2-(Methylenedioxy)-4-aminobenzene			
	0.8 mmol min⁻¹	CO₂	1.0	1% Pd	1:6	140	90	(quantitative)#			
2,4-Di-fluoro-nitrobenzene								2,4-Di-fluoroaniline			
(26)#	0.5	CO₂	1.0	1% Pd	1:2	120	130	(74)#			
Phenyl-aceto-nitrile									Tris-2-phenyl-ethylamine	Ethyl-benzene	Ethyl-cyclo-hexane
(0)#	0.5	propane	1.0	5% Pd	1:4	120	130		(57)#	(36)#	(7)#
(2)#	0.5	propane	1.0	5% Pd	1:6	120	160		(24)#	(58)#	(16)#
(0)#	0.5	propane	1.0	5% Pd	1:8	120	200		(4)#	(55)#	(41)#

Table 1

Substrate	Sub. Flow [ml /min]	Solvent	Flow [l /min]	Catalyst	Substr. :H₂	P_R [bar] (Sol.+H₂)	T [°C]	Products % (analysis by GC (external standards) except when marked with # where analysis is by NMR)			
								2-Propanol	1-Propanol	Acetone	Propanal
Propylene oxide (42)#	0.5	CO₂	1.0	5% Pd	1 : 2	120	120	(49)#	(5)#	(4)#	(0)#
(17)#	1.0	CO₂	1.0	5% Pd	1 : 3	120	250	(22)#	(42)#	(15)#	(4)#
								Cyclo-hexanol	Cyclo-hexanone	Cyclo-hexane	Dicyclohexyl-ether
Cyclo-hexene oxide (6)#	0.5	CO₂	1.0	5% Pd	1 : 2	120	200	(80)#	(9)#	(1)#	(4)#
								Cyclo-hexanol	Phenol		
Cyclo-hexanone (83)#	0.5	CO₂	0.65	3% Ru	1 : 1.5	120	300	(17)#	(0)#		
									3,5,5-trimethyl-cyclo-hexanol	1,1,3-tri-methyl-cyclo-hexane	
Iso-phorone (0)	0.5 - 2.0	CO₂	0.78	5%Pd	1 : 2	120	140-200	(100)	(0)	(0)	
	1.0	CO₂	0.78	5%Pd	1 : 3	200	300	58	22	14	

Table 1

Substrate	Sub. Flow [ml/min]	Solvent	Flow [l/min]	Catalyst	Substr. .: H₂	P_R [bar] (Sol.+H₂)	T [°C]	Products % (analysis by GC (external standards) except when marked with # where analysis is by NMR)			
								Cyclohexanone	Cyclohexane	Benzene	Toluene
Cyclohexanol (25)#	0.5	CO₂	0.65	5%Pd	1:3	120	400	(12)#	(60)#	(3)#	(<0.5)
								3-Methyl-cyclohexanone	3-Methyl-cyclohexanol	Methyl-cyclohexane	Toluene
meta-Cresol (20)	0.5	CO₂	0.65	5%Pd	1:2	120	250	(65)	(14)	(<0.5)	(<0.5)
(0)	0.5	CO₂	0.65	5%Pd	1:5	120	250	(17)	(74)	(5)	(5)
(2)	0.5	CO₂	0.65	5%Pd	1:6	120	400	(5)	(4)	(74)	(15)
								1-Propanol	unidentified product		
Propion-aldehyde (32)	0.5-1.0	CO₂	1.0	5% Ru	1:2.5	120	150	(35)	(33)		
								2-Amino-butane	2-Butanone	2-Butanol	
2-Butanone oxime (4)	0.5	propane	0.75	5% Pt	1:2	80	150-170	(86)	(10)	(<1)	

Flow = Flow rate of fluid in l /min at 20 °C and 1 atm, as determined by flow meter

Catalyst = Deloxan catalyst as presented in Table 2

It is apparent from Table 1 that for a given
reaction medium, variation of the heterogeneous
catalyst and/or the reaction conditions allows control
of the desired end product where there is more than one

5   possible product. Thus, nitrobenzene may be reduced to
aniline, aminocyclohexane or dicyclohexylamine
depending on the pre-determined reaction conditions
which are used. Thus, by changing the temperature of
hydrogenation of nitrobenzene under conditions of

10 excess hydrogen it is possible to influence the
selectivity. The reaction is kinetically controlled
under these conditions and does not depend on mass
transport effects. Similarly, alkynes such as octyne
can be selectively hydrogenated in the process of the

15 present invention by varying the conditions of the
reaction.

Since temperature, pressure and flow rate are
parameters which are readily controlled by an operator,
the present invention enables a particular product to

20 be obtained in good yield in a process which is
commercially viable on account of its safety and ease
of use. Product formation may be monitored in situ by
means of IR spectrometry using a suitably positioned
high pressure IR cell.

25 The present invention will now be described by way
of example only with reference to Figures 1 to 7, in
which:

Figure 1 which is a schematic diagram of a
continuous flow reactor according to the present

30 invention,

Figure 2 shows the possible hydrogenation products
of acetophenone,

Figure 3 shows the relative proportions of the
hydrogenation products of acetophenone at various

35 temperatures with increasing hydrogen,

Figure 4 shows the relative proportions of the

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hydrogenation products of acetophenone at various pressures,

Figure 5 shows the possible hydrogenation products of benzaldehyde,

5   Figure 6 shows the relative proportions of the hydrogenation products of benzaldehyde at various temperatures with increasing hydrogen, and

Figure 7 shows the possible hydrogenation products of nitrobenzene.

10   The organic compound 1, dissolved in an appropriate solvent if it is a solid, is pumped into mixer 2 which may include a stirrer (not shown) where it is mixed with fluid 3 which has been delivered from reservoir 4 via pump 5 to mixer 2. Mixing of organic

15   compound 1 and fluid 3 may equally be effected without the use of a stirrer. Hydrogen 6 is delivered from reservoir 7 via compressor 8 and a dosage unit (e.g. a 6-way injection valve) 9 to mixer 2. The hydrogen pressure is typically set to a pressure of 200 to 220

20   bar inclusive by means of conventional pressure regulating apparatus. Addition of dissolved organic compound 1 and/or hydrogen 6 may be continuous or may occur continuously in a step-wise manner. The hydrogen is added via a switching valve or similar control means

25   to give the required ratio of hydrogen to the organic compound. The ratio of hydrogen to organic compound is chosen according to the reaction to be used and is typically in the range from 1.0 : 1.0, to 3.0 : 1.0, inclusive, equivalents of H_2 per reaction and is

30   preferably set at 1.1 : 1.0 or 1.3 : 1.0 equivalents of H_2 per reaction for optimum results.

The temperature and/or pressure of the mixture of organic compound 1, fluid 3 and hydrogen 6 is adjusted in mixer 2 to a temperature and pressure close to or

35   above the critical point of fluid 3 as required. Heating means or cooling means 10 is provided in mixer

2 for this purpose. Equally, this may be achieved via heating/cooling the reactor or a combination of both. The mixture is then passed into reactor 11 which contains a catalyst (not shown) fixed on a suitable

5   support. Suitable catalysts compose a carrier formed from an organosiloxane-polycondensate, an organosiloxanamine-copolycondensate or polymeric secondary and/or tertiary organosiloxanamine combinations, a metal selected from platinum, nickel,

10   palladium or copper or a mixture thereof, and optionally a promoter. After an appropriate residence time in reactor 11 fluid 3, which contains product 12, is passed into pressure reduction unit 13 and the product is removed via take off tap 14 after passing

15   through pressure reduction unit 13. The flow rate of the reactants through reactor 11 is controlled by a valve (not shown) in pressure reducer 13. The quantity of materials consumed in the reaction and the rate of reaction are determined by the temperature, the feed

20   rate of organic compound 1 into fluid 3 and the flow rate of fluid 3. Fluid 3, together with any unconsumed hydrogen, is vented through relief pipe 15 for subsequent recycling or to the atmosphere.

The parameters of a typical reaction might involve

25   a system pressure of 60 to 140 bar (this will, of course, depend in part on the reaction media), a flow rate of the substrate of 0.5 to 20.0 ml/min, a reactor temperature of 40 to 360°C (again, this will depend in part on the reaction media) and a flow rate of the

30   supercritical or near critical fluid of 0.65 to 1.65 l/min; however, these parameters do not imply limitations to within the respective ranges.

Example 1 - Hydrogenation of Acetophenone

Hydrogenation of acetophenone leads to a variety

35   of products, as illustrated in Figure 2 below. Each of the products can be obtained selectively by appropriate choice of the reaction conditions.

The effect of the reaction temperature on the

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selectivity of the reaction in CO_2 is demonstrated in Figure 3. The pressure of the reaction was maintained at 120 bar and the catalyst was APII 5% Pd Deloxan having a particle size 0.3 to 0.8mm, supplied by

5 Degussa.

The effect of the reaction pressure on the selectivity of the same reaction in CO_2 at a constant temperature of 240°C and using the same catalyst is illustrated in Figure 4.

10 Example 2 - Hydrogenation of Benzaldehyde

Benzaldehyde can be hydrogenated to more than one product, as illustrated in Figure 5, and Figure 6 shows the variation of product selectivity with temperature at a pressure of 120 bar and using an APII 5% Pd

15 Deloxan catalyst having a particle size of 0.3 to 0.8mm, supplied by Degussa.

Example 3 - Hydrogenation of Nitrobenzene

Nitrobenzene may be hydrogenated to a number of products, as illustrated in Figure 7.

20 Table 2 illustrates how the selectivity of the reaction is influenced by small differences in the catalyst at a constant pressure of 80 bar.

Table 2

Catalyst	Temperature °C	Aniline %	Cyclohexylamine %	Dicyclohexylamine %	Cyclohexane %
APII 1% Pd Deloxan	150-200	97	0	0	0
E 8550 P/D 5% Pd Deloxan	200-250	9	29	58	1
APII 5% Pt Deloxan	200	46	13	4	28

Finally, it should be noted that whilst the experiments
described herein represent the most appropriate conditions
for those reactions at the present time, it is nevertheless
envisaged that the yields and selectivities of these
5   reactions may be enhanced further following the principles
of the invention described herein.

Claims:

1.   A process for the selective hydrogenation of one or more functional groups in an organic compound wherein the functional group is selected from: alkene, cyclic alkene, cyclic alkane, lactone, anhydride, amide, lactam, Schiffs base, aldehyde, ketone, alcohol, nitro, hydroxylamine, nitrile, oxime, imine, azine, hydrazone, aniline, azide, cyanate, isocyanate, thiocyanate, isothiocyanate, diazonium, azo, nitroso, phenol, ether, furan, epoxide, hydroperoxide, peroxide, ozonide, arene, saturated or unsaturated heterocycle, halide, acid halide, acetal, ketal, and a selenium or sulfur containing compound, wherein the process consists of continuously hydrogenating the compound over a heterogeneous catalyst where at least one of the components, in addition to hydrogen is under supercritical or near critical conditions, and wherein one or more of temperature, pressure, catalyst, flow rates and hydrogen concentration are controlled so as to effect selective hydrogenation.

2.   A process according to claim 1 characterised in that all the substrate and hydrogen are in a homogeneous single phase with or without an additional solvating fluid.

3.   A process according to claim 1 or 2, wherein the hydrogenation is hydrogenolysis.

4.   A process according to claim 1 or 2, wherein the hydrogenation reaction is the reductive alkylation of primary and secondary amines or ammonia.

5.   A process according to claim 4, wherein the primary or secondary amine is formed in situ before further reaction.

6.   A process according to claim 1 or 2, wherein the hydrogenation reaction is the reductive amination of aldehydes, ketones and phenols.

7.   A process according to claim 6, wherein the carbonyl compound is formed in situ before further reaction with the amine.

8.   A process according to any preceding claim, wherein the organic compound is an aromatic compound.

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9.   A process according to any preceding claim, wherein the supercritical fluid is carbon dioxide, propane, an alkane, an alkene, ammonia, a halocarbon or a mixture of any of these.

5   10.   A process according to any preceding claim, wherein the supercritical fluid is carbon dioxide, propane, or a mixture thereof.

11.   A process according to any preceding claim, wherein the catalyst is a supported metal catalyst.

10   12.   A process according to any preceding claim, wherein the catalyst comprises a carrier formed from an organsiloxane-polycondensate, an organosiloxanamine-copolycondensate or polymeric secondary and/or tertiary organosiloxanamine combinations, a metal selected from platinum, nickel,

15   palladium or copper or a combination thereof, and optionally a promoter.

13.   A process according to any previous claim, wherein the source of hydrogen is an isotope of hydrogen or a hydrogen transfer reagent.
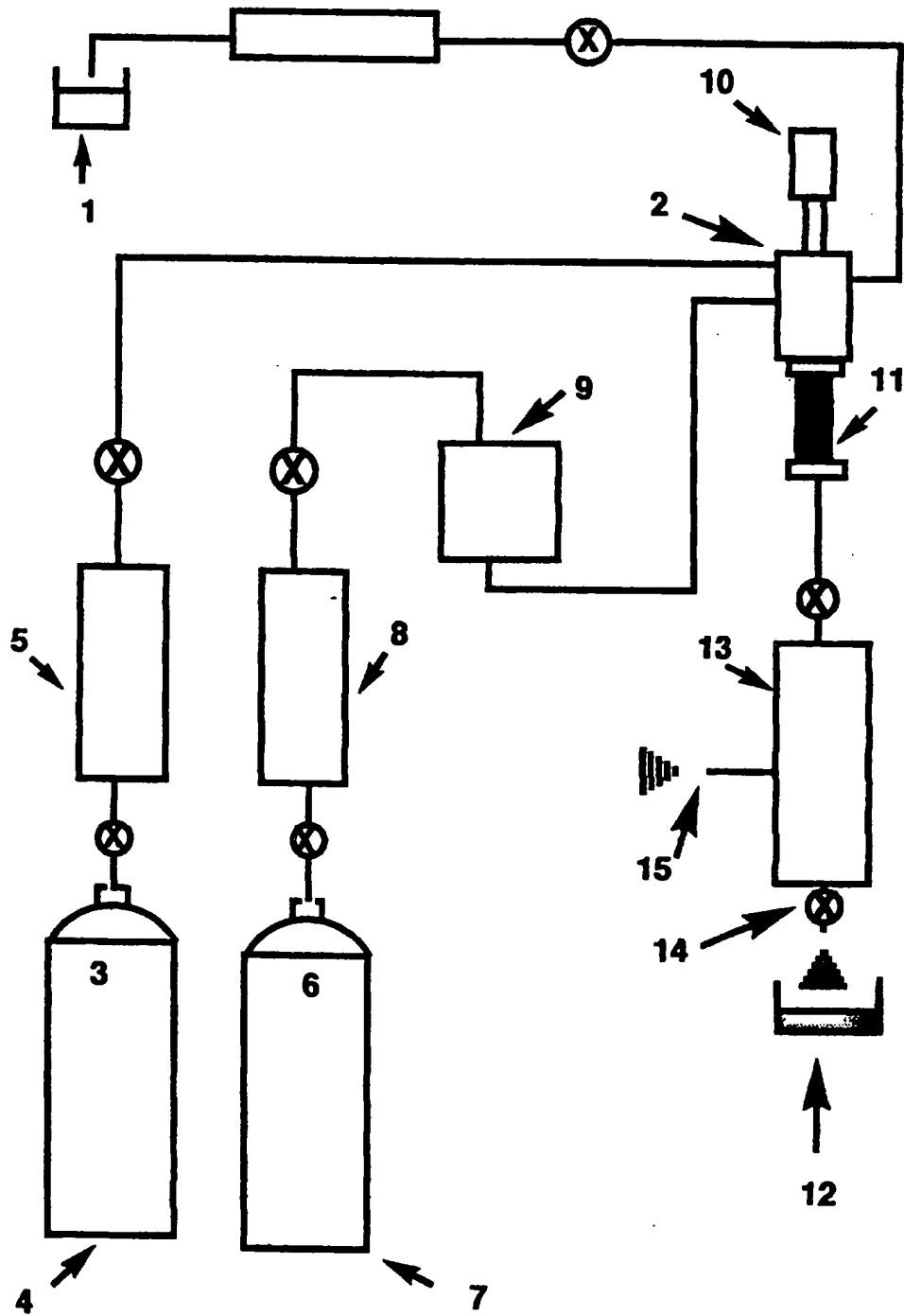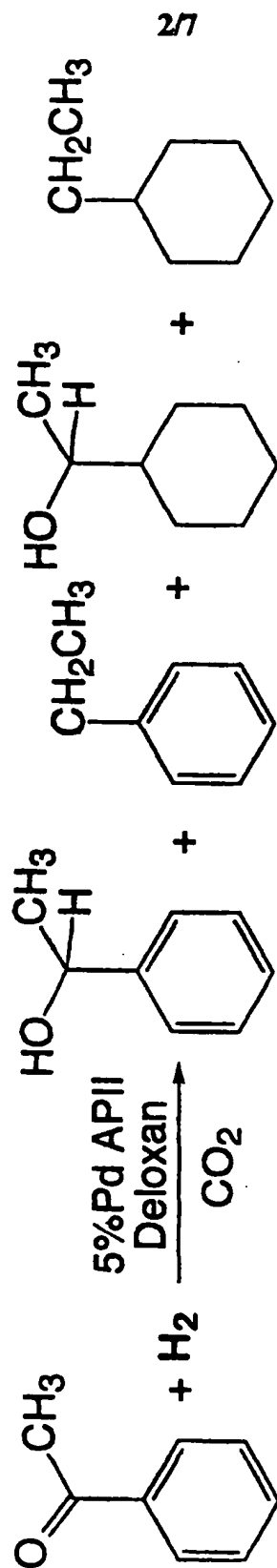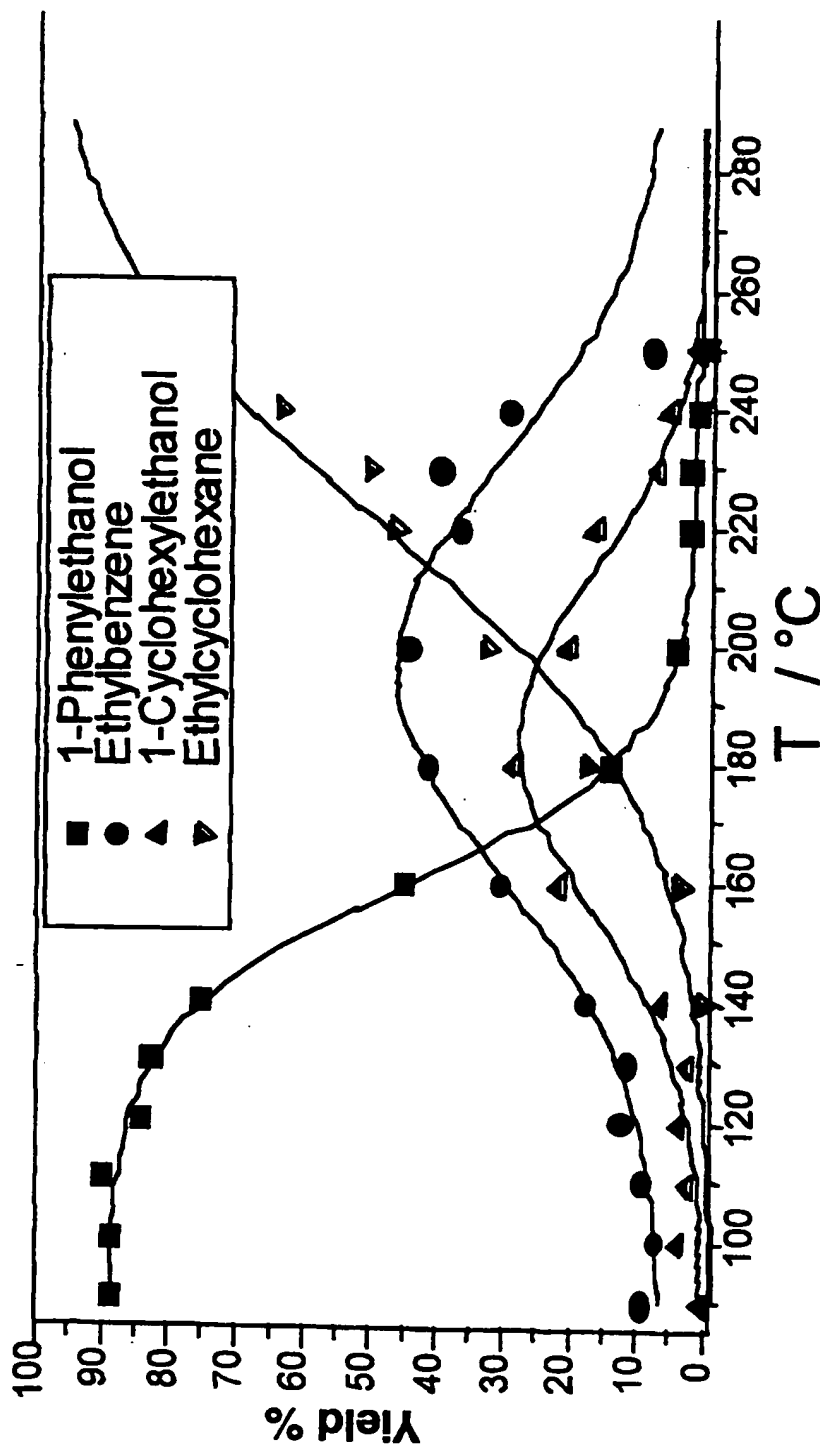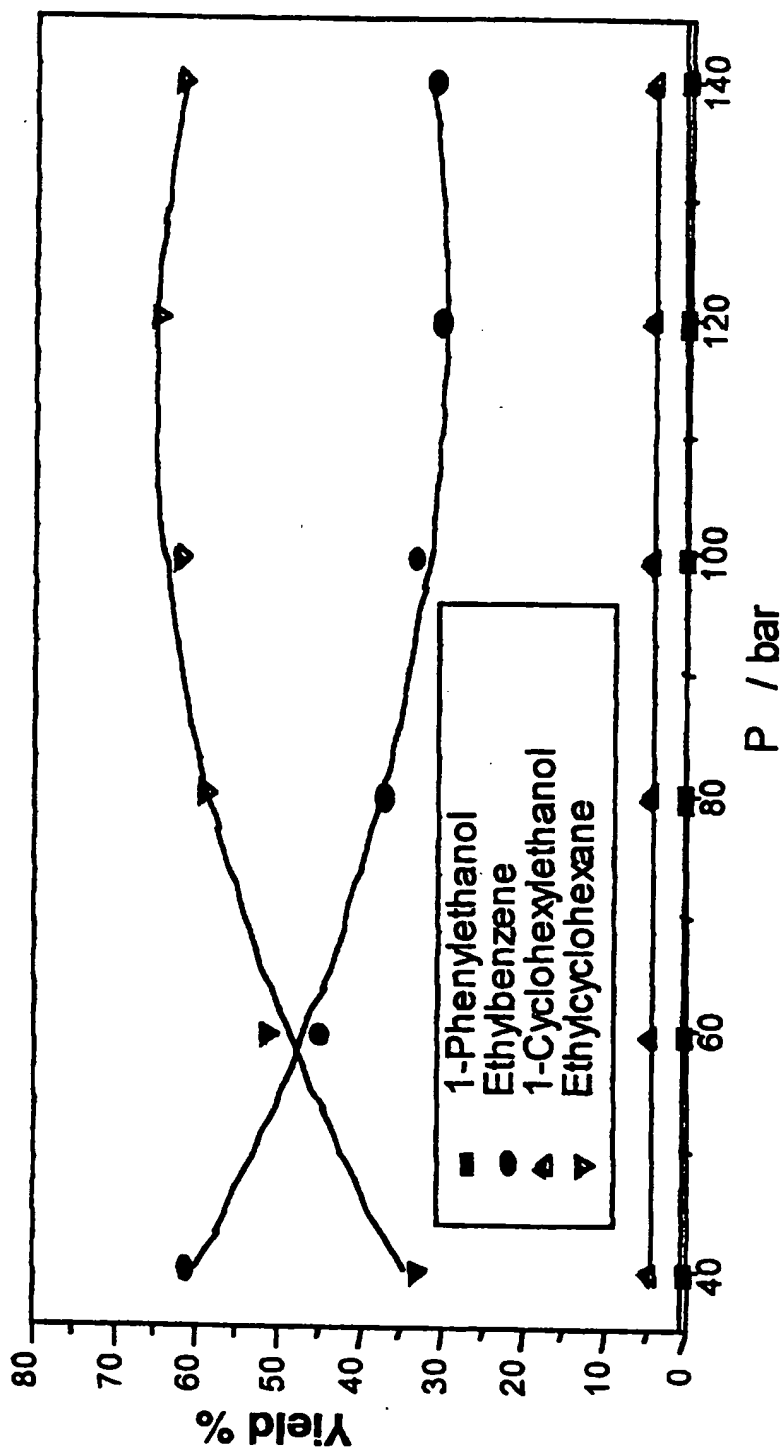
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Figure 1

Figure 2

Figure 3

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Figure 4

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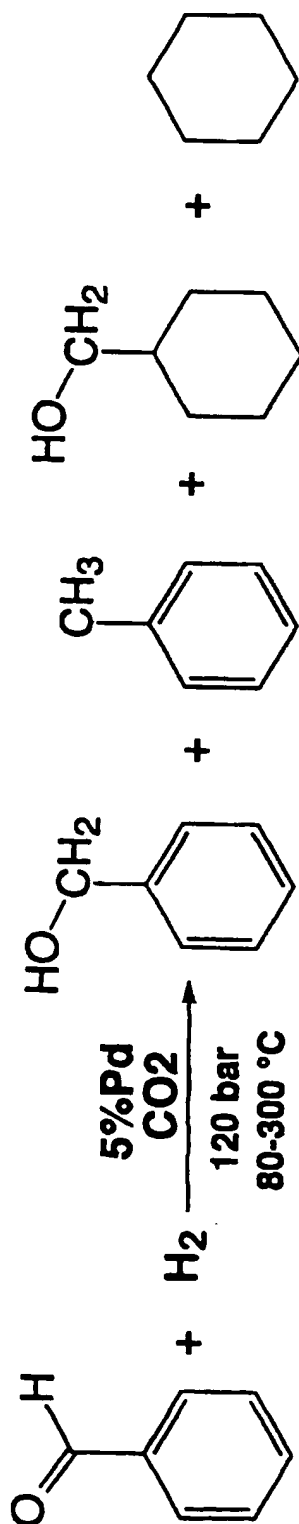
Figure 5
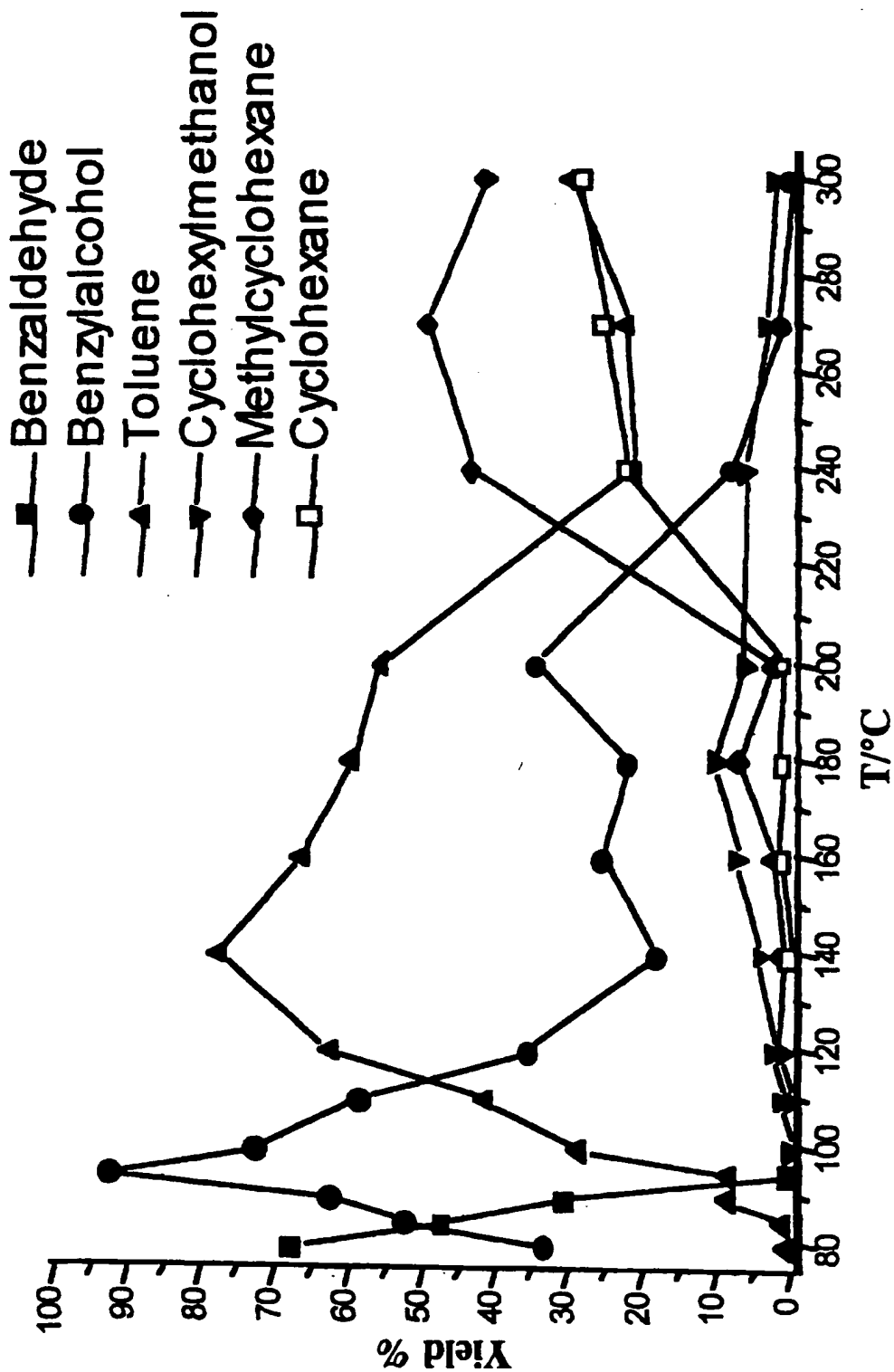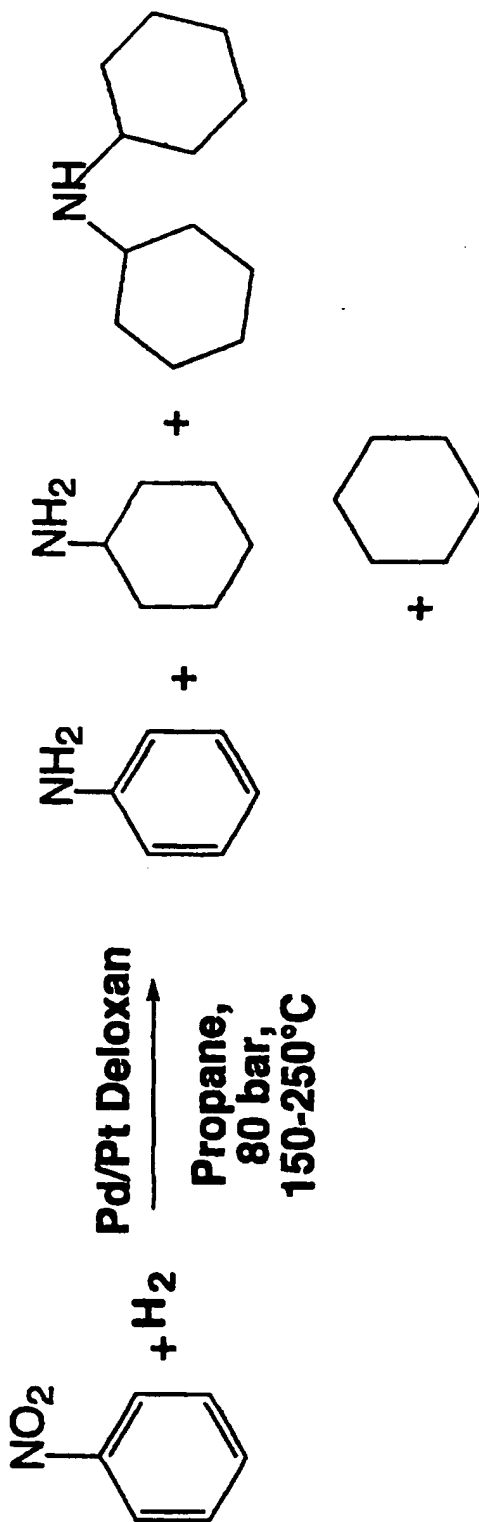
Figure 6

Figure 7

INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6   C07B35/02   C07B43/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6   C07B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96 01304 A (POUL MÖLLER LEDELSES) 18 January 1996 see page 5, line 20 - page 11, line 20; figure 2 ---	1,2,9-12
P,X	PROCESS TECHNOLOGY PROCEEDINGS, vol. 12, 7 October 1996, pages 17-21, XP000676095 T TACKE ET AL: "Hardening of fats and oils in supercritical carbon dioxide" see the whole document ---	1,2,9-12
X	DE 44 05 029 A (DEGUSSA) 24 August 1995 cited in the application see claims; figure 1; examples ---	1,2,9-12

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[X] Further documents are listed in the continuation of box C.   [X] Patent family members are listed in annex.

* Special categories of cited documents :

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
27 June 1997	0 3. 07. 97

Name and mailing address of the ISA	Authorized officer
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 94 06738 A (UNICHEMA CHEMIE) 31 March 1994 cited in the application see page 4, line 17 - page 10, line 11 -----	1-13

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WO 9406738 A	31-03-94	AU	4957193 A	12-04-94